

IN THE CLAIMS

1-100. (cancelled)

101. (previously presented) A recombinant nucleic acid molecule that comprises a vector operatively linked to a nucleic acid according to claim 116, and a promoter suitable for driving the expression of said nucleic acid in a compatible host organism.

102. (previously presented) A recombinant nucleic acid molecule that comprises a vector operatively linked to a nucleic acid according to claim 117, and a promoter suitable for driving the expression of said nucleic acid in a compatible host organism.

103. (previously presented) A recombinant nucleic acid molecule that comprises a vector operatively linked to a nucleic acid according to claim 118, and a promoter suitable for driving the expression of said nucleic acid in a compatible host organism.

104. (original) A host cell transformed with a recombinant nucleic acid molecule according to claim 101.

105. (original) The transformed host cell according to claim 104 wherein said host cell is selected from the group consisting of CHO, VERO or COS cells, *E. coli*, *S. cerivisiae*, *Pichia pastoris typhi*, *S. typhimurium* and a *S. typhimurium-E. coli* hybrid.

106. (original) A host cell transformed with a recombinant nucleic acid molecule according to claim 102.

107. (original) The transformed host cell according to claim 106 wherein said host cell is selected from the group consisting of CHO, VERO or COS cells, *E. coli*, *S. cerivisiae*, *Pichia pastoris typhi*, *S. typhimurium* and a *S. typhimurium-E. coli* hybrid.

108. (previously presented) A host cell transformed with a recombinant nucleic acid molecule according to claim 103.

109. (original) The transformed host cell according to claim 108 wherein said host cell is selected from the group consisting of CHO, VERO or COS cells, *E. coli*, *S. cerivisiae*, *Pichia pastoris typhi*, *S. typhimurium* and a *S. typhimurium-E. coli* hybrid.

110-115. (cancelled)

116. (currently amended) A nucleic acid that encodes a recombinant hepatitis B core (HBc) protein chimer molecule or [[a]] analog or complement thereof, said recombinant HBc protein chimer molecule protein molecule having a length up to about 515 amino acid residues that

(a) contain a sequence of at least about 130 of the N-terminal 150 amino acid residues of the HBc molecule that include one or more peptide-bonded heterologous epitopes at the N-terminus, or in the HBc immunogenic loop or a heterologous

linker residue for a conjugated epitope present in the HBc immunodominant loop,

(b) contain one to ten cysteine residues toward the C-terminus [C-terminal cysteine residue(s)] of the molecule from the C-terminal residue of the HBc sequence and ,within about 30 residues from the C-terminus of the chimera,

(c) contain a sequence of at least 5 amino acid residues from HBc position 135 through position 140 toward the HBc C-terminus, and zero to about 100 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus,

said chimera molecules (i) containing no more than about 5 percent conservatively substituted amino acid residues in the HBc sequence as compared to a sequence of SEQ ID NO:246-251 from position 1 through 149, (ii) self-assembling into particles that are substantially free of binding to nucleic acids on expression in a host cell, and said particles being more stable ~~on storage at 1 mg/mL using 50 mM NaPO<sub>4</sub>, pH 6.8~~ than are particles formed from an otherwise identical HBc chimera that lacks said C-terminal cysteine residue(s) or in which a C-terminal cysteine residue present in the chimera molecule is replaced by another residue, wherein said particle stability is assayed as a measurement of the percentage of full length chimera molecules determined by Coomassie Blue stain of reducing buffer 15%SDS-PAGE results obtained after dilution of purified particles to a concentration of 1 mg/mL in aqueous 50 mM NaPO<sub>4</sub>, pH 6.8, with sodium azide added to a final concentration of 0.02% and incubation at 37° C for about 14 days.

117. (currently amended) A nucleic acid that encodes a recombinant hepatitis B core (HBc) protein chimer molecule or [[a]] analog or complement thereof, said recombinant HBc protein chimer molecule protein molecule having a length of about 135 to about 515 amino acid residues that contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about 71 to about 100 amino acid residues whose sequence includes at least the sequence of the residues of position 5 through position 75 of HBc and optionally includes a heterologous epitope containing up to about 30 amino acid residues peptide-bonded to one of HBc residues 1-4;

(b) Domain II comprises about 5 to about 250 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which (i) at least 4 residues in a sequence of HBc positions 76 through 85 are present peptide-bonded to one to about 245 amino acid residues that are heterologous to HBc and constitute a heterologous epitope or a heterologous linker residue for a conjugated epitope;

(c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

(d) Domain IV comprises (i) 5 through fourteen residues of a HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) one to ten cysteine residues [C-terminal cysteine residue(s)] within about 30 residues from the C-terminus of the chimer molecule, and (iii) zero to about 100 amino acid residues in a sequence heterologous to HBc from

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position 150 to the C-terminus, with the proviso that Domain IV contain at least 6 amino acid residues including said one to ten cysteine residues of (ii), said recombinant chimeric HBc protein molecules being more stable ~~on storage at 1 mg/mL using 50 mM NaPO<sub>4</sub>, pH 6.8~~ than are particles formed from an otherwise identical HBc chimera molecule that lacks said C-terminal cysteine residue or in which a C-terminal cysteine residue present in the chimera molecule is replaced by another residue, wherein said particle stability is assayed as a measurement of the percentage of full length chimera molecules determined by Coomassie Blue stain of reducing buffer 15%SDS-PAGE results obtained after dilution of purified particles to a concentration of 1 mg/mL in aqueous 50 mM NaPO<sub>4</sub>, pH 6.8, with sodium azide added to a final concentration of 0.02% and incubation at 37° C for about 14 days, and having an amino acid residue sequence in which no more than about 5 percent of the amino acid residues are conservatively substituted in the HBc sequence as compared to a sequence of SEQ ID NO:246-251 from position 1 through 149.

118. (currently amended) A nucleic acid that encodes a recombinant hepatitis B core (HBc) protein chimera molecule or [[a]] analog or complement thereof, said recombinant chimeric HBc protein molecules having a length of about 175 to about 240 amino acid residues and contain four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about the sequence of the residues of position 1 through position 75 of HBc;

(b) Domain II comprises about 5 to about 55 amino acid residues peptide-bonded to HBc residue 75 of Domain I in which

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at least 4 residues in a sequence of HBc positions 76 through 85 are present peptide-bonded to 6 to about 50 amino acid residues that are heterologous to HBc and constitute a heterologous epitope;

(c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

(d) Domain IV comprises (i) 5 through fourteen residues of a HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) a cysteine residue [C-terminal cysteine residue] within about 30 residues from the C-terminus of the chimera molecule, and (iii) zero to about 50 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus,

said chimera self-assembling into particles on expression in a host cell that exhibit a ratio of absorbance at 280 nm to 260 nm of about 1.2 to about 1.6 and are more stable ~~on storage at 1 mg/mL using 50 mM NaPO<sub>4</sub>, pH 6.8~~ than are particles formed from an otherwise identical HBc chimera molecule that lacks said C-terminal cysteine residue or in which a C-terminal cysteine residue present in the chimera molecule is replaced by another residue, , wherein said particle stability is assayed as a measurement of the percentage of full length chimera molecules determined by Coomassie Blue stain of reducing buffer 15%SDS-PAGE results obtained after dilution of purified particles to a concentration of 1 mg/mL in aqueous 50 mM NaPO<sub>4</sub>, pH 6.8, with sodium azide added to a final concentration of 0.02% and incubation at 37° C for about 14 days, and having an amino acid residue sequence in which no more than about 5

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percent of the amino acid residues are conservatively substituted in the HBc sequence of the chimera as compared to a sequence of SEQ ID NO:246-251 from position 1 through 149.

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